CARDIOVASCULAR SCIENCES IRG

OVERALL DESCRIPTION

The Cardiovascular Sciences (CVS) IRG will consider research applications that employ basic investigations, translational approaches and patient-oriented studies to focus on the development, physiology, and pathophysiology of the heart and circulatory systems. Study sections are organized around themes of development, muscle contraction including cardiac hypertrophy and failure, cardiovascular electrophysiology and arrhythmias, myocardial ischemia and infarction, vascular hemodynamics and hypertension, neural and integrative, systems physiology, inflammation and atherosclerosis, and vascular cell and molecular biology. Investigators may employ a range of approaches that include genetics, genomics and proteomics, molecular, cell, and computational biology, biochemistry, biophysics and bioengineering, imaging, analyses of model organisms, and human studies.

Study sections in the CVS IRG include:

- Cardiovascular Differentiation and Development (CDD)
- Cardiac Contractility, Hypertrophy and Failure (CCHF)
- Electrical Signaling, Ion Transport and Arrhythmias (ESTA)
- Vascular Cell and Molecular Biology (VCMB)
- Myocardial Ischemia and Metabolism (MIM)
- Hypertension and Microcirculation (HM)
- Atherosclerosis and Inflammation of the Cardiovascular System (AICS)
- Clinical and Integrative Cardiovascular Sciences (CICS)

The study sections that compose the CVS IRG are amongst the first to be proposed for re-organization and implementation. As a result, some of the Teams that will develop recommendations for other IRGs that may share interests in areas of research with the CVS IRG have not yet met or completed their deliberations. Therefore, the proposed "shared interest" guidelines for each of the study sections listed below are tentative, pending further input from the remaining study section design Teams, the community, and the CSR Advisory Committee to the Director, CSR

Cardiovascular Differentiation and Development (CDD) Study Section

The Cardiovascular Differentiation and Development (CDD) study section reviews applications concerning normal and abnormal development and differentiation of the heart, vascular and lymphatic systems. This focus includes stem and progenitor cells, tissue interactions, morphogenetic processes, and regulation of differentiation in humans and model organisms.

Specific areas covered by CDD:

- Cardiac development, including commitment and differentiation of cell
 phenotypes, cardiac lineages, cardiac transcription factors and their coactivators
 or repressors, developmental regulation of RNA splicing and developmental
 changes in protein isoform expression.
- Cardiac morphogenesis, including looping morphogenesis, chamber specification, positional information as it relates to the developing heart, valve morphogenesis and changes in cell number, shape or survival in the context of heart formation.
- Development and differentiation of the conduction system in the heart.
- Neural crest contributions to the heart and great vessels in developing organisms.
- Vascular development, including the origin, commitment and differentiation of endothelial and smooth muscle cell populations. Cell-cell and tissue interactions that regulate vasculogenesis and angiogenesis, cell polarity and organization. Inductive stimuli that regulate differentiation and gene expression. Patterning components that regulate the position, size and organization of the vascular system. Aspects of smooth muscle that include different embryonic origins and divergent physiological responses based on origins.
- Development of the coronary circulation and the epicardium.
- Vascular remodeling in the postnatal organism where angiogenic stimuli produce new outgrowth and vascularization in a recapitulation of embryonic and fetal processes.
- Studies of lymphangiogenesis including the origins, commitment, differentiation and organization of the lymphatic vascular system. This does not include components of the immune system found in the lymphatic drainage system.
- Embryonic cell processes including migration, chemotaxis, cell-cell adhesion, extracellular matrix adhesion, secretion or modification, organization of the cytoskeleton or sarcomere and apoptosis will be covered as they are related to development and differentiation of the cardiovascular system.
- Receptors, signaling, gene regulation and protein expression as related to the differentiation and development of the embryonic and fetal cardiovascular systems.
- Stem cell biology related to the cardiovascular system including differentiation of embryonic and adult stem cells into cardiomyocytes, endothelium, smooth muscle and other components of the cardiovascular system. Characterization of endogenous stem cells that contribute to the myocardium and vasculature in vivo. Genetic and pharmacologic enhancements to stem cells to promote their accessibility, function or usefulness.
- Studies of cardiovascular development in a variety of model organisms, including Drosophila, Xenopus, zebrafish, chick and mouse.
- Studies related to the understanding of human congenital cardiac and vascular malformations, including valvular and septal defects, chamber malformations, maternal-fetal vascular connections, teratologic mechanisms, and fetal cardiac pathology.
- Genomic and proteomic approaches to cardiovascular development including expression profiling, mapping of protein interaction networks, saturation

- mutagenesis and high throughput phenotyping, and the functional evaluation of changes in normal and abnormal development.
- Human genetics of cardiac and vascular malformations, including positional cloning, structure-function and genotype-phenotype correlations, and the modeling of human developmental cardiovascular disorders in other organisms.

Shared Interest Within IRG:

- <u>Cardiac Contractility</u>, <u>Hypertrophy and Failure (CCHF)</u>: Applications addressing calcium regulation and receptor-mediated effects restricted to myocyte growth signaling, contractility, apoptosis, and remodeling are appropriate for review by CCHF. The renin/angiotensin system as it relates to cellular growth is also appropriate for assignment to CCHF. Embryonic growth and differentiation of myocytes is more appropriately assigned to CDD.
- <u>Electrical Signaling</u>, <u>Ion Transport and Arrhythmias (ESTA)</u>: Applications that deal with congenital and acquired arrhythmia syndromes and other ion movement abnormalities may be assigned to ESTA, while studies focusing on development of electrically active cells will be assigned to CDD.
- <u>Vascular Cell and Molecular Biology (VCMB):</u> Applications that focus on elements of blood vessel growth and differentiation in postnatal vascular beds may be assigned to VCMB. Embryonic growth and differentiation of vessels is more appropriately assigned to CDD.

- Genes, Genomes & Genetics (GGG) IRG: Shared interests occur in genetic
 analysis of cardiac and vascular malformations. When the focus is a general
 genetic understanding, assignment could be to the GGG IRG. When the focus is
 an understanding of the biology and physiology of the cardiovascular system,
 assignment could be to CDD.
- Molecular Approaches to Cell Function and Interactions (MACFI) IRG: Shared interests occur in cellular and molecular examination of developing cardiovascular tissues. When the focus is a general cellular or molecular understanding, assignment could be to the MACFI IRG. When the focus is an understanding of the biology and physiology of the cardiovascular system, assignment could be to CDD.
- Biology of Development and Aging (BDA) IRG: Shared interest exists in the areas of organogenesis, including birth defects. In general, applications that focus on early developmental processes up to and including formation of the primordial heart, blood and vasculature, and malformations which emerge at these earlier stages, would typically be assigned to the BDA IRG. On the other hand, applications with a focus on developmental events after formation of these primordial tissues, including birth defects, would typically be assigned to CDD. The BDA IRG may also be assigned applications that study post-primordial developmental events when the purpose of the study is to uncover or further elucidate common fundamental developmental processes. An example would be

where the focus is on processes common to various mesodermal derivatives. Assignment would be made based on the central focus of the application.

- Oncological Sciences (ONC) IRG: Shared interest exists in the area of angiogenesis. Where studies focus on developmentally related processes or reactivation of embryonic processes they could be assigned to CDD. When the focus is on tumor angiogenesis assignment to the ONC IRG would be appropriate.
- Hematology (HEM) IRG: Shared interest may exist concerning common stem cell precursors of the endothelial and hematopoetic cell types. While studies of multipotent or bipotent stem cells could be assigned to CDD, hematopoetic differentiation may be more appropriately assigned to the HEM IRG. Assignment of applications on the transdifferentiation of cells between the blood and endothelial cell types would be resolved in the direction of the final phenotype.

Cardiac Contractility, Hypertrophy, and Function (CCHF) Study Section

The Cardiac Contractility, Hypertrophy, and Function (CCHF) study section reviews applications involving both basic and applied aspects of the heart that focus on contractile function and dysfunction, including studies of hereditary and acquired cardiac hypertrophy and failure, at levels ranging from molecular assemblies to the intact organ.

Specific areas covered:

- Cardiac hypertrophy and adaptation to abnormal hemodynamic load; mechanical signal transduction, genetic myopathies (hypertrophic, dilated, and metabolic), autocrine/paracrine factors; apoptosis; cell cycle factors; aging inflammatory/cytokine-mediated processes; transcriptional pathways in heart failure; capillary density; transition from compensated to uncompensated state.
- Systolic and diastolic dysfunction and heart failure, including: molecular and cellular mechanisms of heart failure; remodeling and extracellular matrix reorganization; capillary density; metabolic adaptations; myocyte energetics; aging.
- The cytoskeleton including biochemistry, transport functions, molecular biology and biophysical aspects of myocyte and ventricular mechanics.
- Genomic and proteomic approaches to cardiac hypertrophy and failure including expression profiling and functional consequences of the changes; genotypephenotype correlation in human and model organisms.
- Studies of cardiac repair including cell-based therapy.
- Neurohumoral and receptor mechanisms as they relate to hypertrophy and heart failure including adrenoreceptors, cytokines and growth factor receptors.
- Studies of cardiac myocyte contractile function including sarcomeric proteins, isoforms of these proteins; structural elements in normal and disease states, calcium-force relationship; structure-function relationship of sarcomeric proteins.
- Ventricular mechanics; stress-strain relationships; tissue mechanics and constitutive properties of myocardium; myofiber orientation; fibrosis; assessment

of the effects of therapeutic interventions such as pacing, ventricular assist devices and others.

- Calcium regulation, signaling as it relates to contractility, diastolic function and relaxation.
- Receptor and post-receptor signaling for control of myocyte growth, remodeling and contractility.
- Valvular heart disease with or without hemodynamic dysfunction.
- Arrythmia-related causes of remodeling and heart failure.
- Acute and chronic changes in ventricular and cellular function that result from heart transplantation.

Shared Interests Within the IRG:

There is a shared interest in heart failure signaling, arrhythmias and transplantation with other study sections in this IRG. Specific shared interests may occur with applications addressing:

- <u>Cardiovascular Differentiation and Development (CDD):</u> Embryonic growth and
 differentiation of myocytes is appropriately assigned to CDD. Applications
 addressing calcium regulation and receptor-mediated effects restricted to
 myocyte growth signaling, contractility, apoptosis, and remodeling are more
 appropriate for review by CCHF. The renin/angiotensin system as it relates to
 cellular growth is also appropriate for assignment to CCHF.
- <u>Electrical Signaling</u>, <u>Ion Transport and Arrhythmias (ESTA)</u>: The study of arrhythmias occurring as a consequence of heart failure and other arrhythmia related studies should be assigned to ESTA. When arrhythmias are studied as an etiology of heart failure and myocardial remodeling, including therapeutic effects of pacing on ventricular hemodynamics, the application is appropriately assigned to CCHF.
- Myocardial Ischemia and Metabolism (MIM): Transplant related organ preservation is more appropriately assigned to MIM. Applications that study inflammation of the myocardium secondary to ischemia and the role of reactive oxygen and nitrogen species, cytokines, and chemokines in myocardial ischemia/reperfusion injury are appropriately assigned to MIM. When transplantation is studied only in relation to assessment of myocardial function, applications may be assigned to CCHF.
- Atherosclerosis and Inflammation of the Cardiovascular System (AICS):
 Transplantation biology including transplant related arrhythmias, graft vasculopathy, atherosclerosis, and transplant immunobiology are appropriately assigned to AICS. When transplantation is studied only in relation to assessment of myocardial function, applications may be assigned to CCHF.
- <u>Clinical and Integrative Cardiovascular Sciences (CICS)</u>: Clinical, population, and integrative studies may be more appropriately assigned to CICS.

- Genes, Genomes & Genetics (GGG) IRG: Shared interests include genetic analysis of contractile function or dysfunction. When the focus is a general genetic understanding, assignment could be to the GGG IRG. When the focus is an understanding of the biology and physiology of the cardiovascular system, assignment could be to CCHF.
- Molecular Approaches to Cell Function and Interactions (MACFI) IRG: Shared interests include cellular and molecular examination of contractility and hypertrophy. When the focus is a general cellular or molecular understanding, assignment could be to the MACFI IRG. When the focus is an understanding of the biology and physiology of the cardiovascular system, assignment could be to CCHF.
- Biology of Development and Aging (BDA) IRG: Studies on aging where the primary focus is on ventricular mechanics, myocyte function (systolic and diastolic), or genetic adaptations affecting contractile function, could be assigned to CCHF. Studies on the cardiovascular system that are testing hypotheses about mechanisms of aging that affect multiple systems or non-cardiovascular tissues could be assigned to the BDA IRG. Studies on cardiovascular function or properties that are part of studies of multiple age-related changes in physiology or body composition (e.g., fat, cardiovascular and bone) could be assigned to the BDA IRG
- Endocrinology, Metabolism, Nutrition and Reproductive Sciences (EMNR) IRG:
 Studies relating to cardiac metabolism as a chronic adaptation to obesity,
 diabetes or diet leading to cardiac hypertrophy and heart failure may be
 assigned to CCHF. Proposals that focus primarily upon the effects of obesity,
 diabetes, or dietary changes on the whole body or multiple organ systems are
 appropriate for the EMNR IRG.
- <u>Surgical Sciences</u>, <u>Biomedical Imaging and Bioengineering (SBIB) IRG</u>: There is significant shared interest with the SBIB IRG. Areas such as organ preservation and graft rejection-related arrhythmias, and surgical interventions to treat valve dysfunction, may be assigned to the SBIB IRG. The responses of the cardiovascular system to trauma, surgery, or other physiologic stress may be assigned to CCHF.

Electrical Signaling, Ion Transport, and Arrhythmias (ESTA) Study Section

The Electrical Signaling, Ion Transport, and Arrhythmias (ESTA) study section will examine both basic and clinical applications related to cardiac and vascular electrical activity, excitation-contraction coupling, and related signaling. This study section reviews applications that address the occurrence, cause, and treatment of cardiac and vascular electrical and electromechanical dysfunction, arrhythmias, and sudden death. Studies may involve animals and humans, *in vitro* and *in vivo* systems, and computational approaches. Where appropriate, studies will be considered that examine the effects of aging on arrhythmias, calcium homeostasis, and excitability.

Specific Areas Covered:

- Structure-function of ion channels in membranes (cell surface and sarcoplasmic reticulum).
- Biophysical and other approaches to study the function of individual protein molecules (e.g., ion channels, connexins, and excitation-contraction (EC) coupling proteins).
- Regulation of expression and function of molecules that determine electrical activity, including their transcriptional regulation, post-translational modifications, assembly, trafficking, and anchoring.
- Basis of propagation and repolarization in normal and diseased hearts, including studies of specialized conduction systems and molecules such as connexins involved in cell-cell communication.
- Functional consequences of disease-associated mutations in ion channel and other genes that result in arrhythmias and vascular cell dysfunction.
- Identification of novel genes and proteins that modulate cardiac and vascular electrical activity, excitation-contraction coupling, and related signaling.
- Altered electrical behavior in acquired heart disease; *e.g.* remodeling related to arrhythmias, heart failure, hypertrophy, or ischemia.
- Intracellular calcium homeostasis (uptake and release mechanisms) and its role in calcium-related arrhythmias, and cardiac and VSM contractility.
- Calcium regulation of receptors, channels, transporters, and other calciumsensitive proteins.
- Excitation-contraction and electromechanical coupling.
- Mediators and modulators of EC coupling, basis of action of individual components of EC coupling.
- Predictors of arrhythmias, including electrocardiography, body surface mapping, intracardiac recordings, signal averaging, and others.
- Computational techniques to model individual channel activity in cellular and multicellular preparations, including the whole heart.
- Technique and device development for treatment of heart rhythm disorders.
- Evaluation of devices that are used in diagnosis and therapy of cardiac rhythm disorders.
- Identification and evaluation of pharmacologic and non-pharmacologic antiarrhythmic interventions.

Shared Interests Within the IRG:

There is a shared interest in ion transfer and transport mechanisms affecting electrical activity and EC-coupling as a common endpoint for pathological conditions, with other study sections in this IRG. Applications that deal specifically with cardiac and vascular electrical activity, excitation-contraction coupling and related signaling, and electrophysiologic aspects of disease processes will most properly be assigned to the ESTA study section. Specific shared interests may occur with:

 <u>Cardiovascular Differentiation and Development (CDD):</u> Studies focusing on development of electrically active cells will be assigned to CDD. ESTA will review those applications that deal with congenital and acquired arrhythmia syndromes and other ion movement abnormalities.

- Cardiac Contractility, Hypertrophy, and Function (CCHF): When arrhythmias are studied as an etiology of heart failure and myocardial remodeling, including therapeutic effects of pacing on ventricular hemodynamics, the application is appropriately assigned to CCHF. ESTA will review applications that focus primarily on ion-movement, calcium homeostasis, and arrhythmias in hypertrophy, heart failure, ischemia, and transplant. Applications with a primary focus on modification of proteins involved in excitability by activation of signaling pathways in these conditions will also be assigned to ESTA.
- <u>Vascular Cell and Molecular Biology (VCMB):</u> VCMB reviews those applications that emphasize a coupling to vascular cell and molecular biology. Applications dealing with the electrical consequences of hypertension, receptors, reninangiotensin system in the heart and vasculature will be assigned to ESTA. Fundamental studies of ion channels or calcium homeostasis without reference to integrated vascular cell function might be more appropriately assigned to the ESTA.
- Clinical and Integrative Cardiovascular Sciences (CICS): CICS may
 appropriately be assigned those applications that deal with arrhythmogenesis
 and are outcome based. Applications that deal with the mechanism of
 arrhythmogenesis are the purview of ESTA.

- Biological Chemistry and Macromolecular Biophysics (BCMB) IRG: Studies
 focusing on molecules involved in cardiac and vascular electrical activity,
 excitation-contraction coupling, and related signaling may be assigned to ESTA,
 whereas those developing methods or using these molecules simply as reagents
 may be assigned to the BCMB IRG.
- Molecular Approaches to Cell Function and Interactions (MACFI) IRG: Studies
 using molecular approaches to evaluate electrical and electromechanical
 functions and interactions in the cardiovascular system could be assigned to
 ESTA. Alternatively, studies using molecular approaches to derive more general
 knowledge of electrical and electromechanical function could be assigned to the
 MACFI IRG.
- Genes, Genomes & Genetics (GGG) IRG: Studies focusing on genetic, genomic
 or proteomic approaches to identification and characterization of genes or
 pathways involved in electrical and electromechanical function in the
 cardiovascular system could be assigned to ESTA. If the studies propose to use
 genetic and genomic approaches to identify and characterize such genes, but the
 focus extends beyond the cardiovascular system, or have a general focus on
 basic mechanisms of electrical or electromechanical function, they could be
 assigned to the GGG IRG.
- <u>Biology of Development and Aging (BDA) IRG:</u> Studies on aging where the
 primary focus is on cardiovascular electrical activity could be assigned to ESTA.
 Studies on the cardiovascular system that are testing hypotheses about
 mechanisms of aging that affect multiple systems or non-cardiovascular tissues

could be assigned to the BDA IRG. Studies on cardiovascular function or properties that are part of studies of multiple age-related changes in physiology or body composition (e.g., fat, cardiovascular and bone) could be assigned to the BDA IRG

- Bioengineering Sciences and Technologies (BST) IRG: Applications to develop fundamental bioengineering methods, pharmacologic and non-pharmacologic interventions, and computational/modeling approaches could be assigned to the BST IRG, whereas those proposing development and validation of methods focusing on evaluation of cardiac and vascular electrical activity, excitationcontraction coupling, and related signaling could be assigned to ESTA.
- <u>Digestive Sciences (DIG) IRG:</u> Studies that examine arrhythmias due to administration of therapeutic agents may be assigned to ESTA. Applications that focus on the general disposition of pro-drugs and drugs or biopharmaceutical agents, and their mechanisms of action may be assigned to the DIG IRG.
- Respiratory Sciences (RES) IRG: Studies of the electrophysiology of pulmonary vasculature could be assigned to ESTA while studies of the consequences of altered electrical behavior in the pulmonary circulation could be assigned to the RES IRG.
- Surgical Sciences, Biomedical Imaging and Bioengineering (SBIB) IRG:
 Applications to develop fundamental imaging methods or early stages of development of sensors may be assigned to the SBIB IRG, whereas those proposing development and validation of methods focusing on evaluation of cardiovascular electrical activity could be assigned to ESTA. Studies of arrhythmias associated with cardiac surgery or cardiopulmonary bypass can be appropriately assigned either in the SBIB IRG or to ESTA, with ESTA focused more on cardiovascular evaluation.

Vascular Cell and Molecular Biology Study Section (VCMB) Study Section

The Vascular Cell and Molecular Biology (VCMB) study section reviews applications involving the cell and molecular biology of blood vessels ranging from major arteries to the microcirculation. Studies using cellular, biochemical, biophysical, immunological, genetic, pharmacological, and molecular biological approaches to define vascular homeostasis and dysfunction are reviewed. A principal focus is on the biology of the endothelium, vascular smooth muscle cell, as well as adventitial cells and pericytes.

Specific areas covered:

 Vascular homeostasis: growth control; apoptosis; cell differentiation; senescence; extracellular matrix; receptor biology; electrophysiology; signaling pathways; intercellular communication.

- Transcription, gene regulation as they relate to vascular biology: transcription factors; promoter analyses; genomics; microarrays; bioinformatics; gene clustering.
- Posttranscriptional regulation including mRNA stability, translational control and posttranslational modification including phosphorylation, lipid modification and ubiquitination as they relate to vascular homoeostasis.
- Protein biochemistry of the vascular cell: protein-protein interactions; protein structure; structural biology; proteomics
- Vasomotor activity: vasocontraction and relaxation; nitric oxide; archidonic acid metabolites; endothelins; reactive oxygen and nitrogen species; Endothelial-Derived Hyperpolarizing Factor(s).
- Leukocyte trafficking in vascular homeostasis: leukocyte rolling and trafficking; adhesion molecules; chemokines; cytokines; intercellular signaling.
- Injury / repair: remodeling; angioplasty; restenosis; grafts; stents; reendothelialization; stem cells; novel interventional therapies and evaluation of established devices.
- Mechanotransduction: hemodynamic forces; stress/strain; force transmission coupling in cells; mechanosignaling.
- Endothelial barrier function: permeability and transport; permeability factors; cell junctions; transmigration; extracellular matrix-mediated signaling; reactive oxygen and nitrogen species.
- Vascular contribution and response to coagulation: thrombosis and fibrinolysis mechanisms mediated by the vascular cells; platelet-endothelial interactions; tissue factor.
- Cellular dynamics through imaging: 3-D imaging; fluorescent fusion proteins; cytoskeleton; organelle dynamics; vesicular traffic.

Shared Interests Within the IRG:

There is a shared interest in the elements of vascular cell biology with other study sections in this IRG. Specific shared interests may occur with:

- <u>Cardiovascular Differentiation and Development (CDD):</u> Embryonic growth and differentiation of vessels is more appropriately assigned to CDD. VCMB reviews elements of blood vessel growth and differentiation in postnatal vascular beds.
- <u>Electrical Signaling, Ion Transport, and Arrhythmias (ESTA):</u> Fundamental studies of ion channels or calcium homeostasis without reference to integrated vascular cell function might be more appropriately assigned to ESTA. VCMB reviews those applications that emphasize a coupling to vascular cell and molecular biology.
- Hypertension and Microcirculation (HM) or Clinical and Integrative
 <u>Cardiovascular Sciences (CICS)</u>: Applications addressing integrated and regional microvasculature function are appropriately assigned to HM or CICS.
 VCMB focuses more on studies of the microcirculation at the cell and molecular levels.
- Atherosclerosis and Inflammation of the Cardiovascular System (AICS): Studies
 of atherogenesis or vasculitis are more appropriately assigned to AICS.

Clinical and Integrative Cardiovascular Sciences (CICS): Patient-oriented and
whole animal research on the use of stents, pacemakers, etc. in vascular injury
and repair are appropriate for CICS. Studies on vascular repair and injury where
the focus is at the cell and molecular levels may be assigned to VCMB.

- Molecular Approaches to Cell Function and Interactions (MACFI) IRG: Shared interests concern cellular and molecular examination of vascular structure/function. When the focus is a general cellular or molecular understanding, assignment could be to the MACFI IRG. When the focus is an understanding of the biology and physiology of the cardiovascular system, assignment could be to VCMB.
- Genes, Genomes & Genetics (GGG) IRG: Shared interests concern genetic
 analysis of vascular homeostasis or dysfunction. When the focus is a general
 genetic understanding, assignment could be to the GGG IRG. When the focus is
 an understanding of the biology and physiology of the cardiovascular system,
 assignment could be to VCMB.
- <u>Bioengineering Sciences and Technologies (BST) IRG:</u> Proposals on bioengineering related specifically to devices, gene therapy, and computational modeling approaches for cardiovascular disease (stents, pacemakers, etc.) and their use in cardiovascular injury and repair may be assigned to VCMB. Those involving more general aspects of devices, gene therapy, and computational modeling approaches could be assigned to the BST IRG or the SBIB IRG.
- Immunology (IMM) IRG: Applications focusing on endothelial cell activation could be assigned to VCMB. Applications focusing on leukocyte biology could be assigned to the IMM IRG.
- Hematology (HEM) IRG: The interaction of blood elements with the vascular wall is complex and represents an area of shared interest. Assignment to the HEM IRG may be appropriate when the application is focused on: (1) vessel wall interactions with blood elements, including responses to shear stress, when the primary focus is on the biology of the formed blood elements, (2) soluble angiogenic factors from blood in regulating endothelial cell growth and function, or (3) the biology of soluble and formed blood elements in thrombosis.

 Assignment to VCMB may be appropriate when the focus is on: (1) vessel wall interactions with blood elements, including responses to shear stress, when the primary focus is on the biology of the vascular wall and extracellular matrix, including lipoprotein biology and atherogenesis, (2) vascular wall elements and the extracellular matrix in regulating endothelial cell growth and function including embryonic development of the vasculature, or the role of the vessel wall elements in non-tumor associated angiogenesis, or (3) the vascular wall and extracellular matrix in thrombosis and hemostasis.

- Respiratory Sciences (RES) IRG: In general, applications on vascular cell biology could be assigned to VCMB. Studies related specifically to the vascular biology of the pulmonary system would, in general, be assigned to the RES IRG.
- Surgical Sciences, Biomedical Imaging and Bioengineering (SBIB) IRG: The use
 of imaging to study vascular cell properties and dynamics is appropriate for
 VCMB. The development of imaging technologies is appropriate for the SBIB
 IRG. Proposals on bioengineering related specifically to devices for
 cardiovascular disease (stents, pacemakers, etc.) and their use in cardiovascular
 injury and repair are appropriate for VCMB. Those involving more general
 aspects of bioengineering could be assigned to the BST IRG or the SBIB IRG.

Myocardial Ischemia and Meatbolism (MIM) Study Section

The Myocardial Ischemia and Metabolism (MIM) Study Section reviews applications involving basic and applied aspects of myocardial ischemia/reperfusion (regional or global), coronary circulation, and myocardial metabolism. Studies using molecular, genetic, cellular, biochemical, pharmacological, genomic, proteomic, and physiological approaches to define normal and pathological processes and to develop therapeutic strategies are reviewed. MIM examines investigations at all levels of organization, ranging from in vitro models of simulated ischemia in isolated cells to whole animal models.

Specific areas covered:

- Regional and global myocardial ischemia/reperfusion: mechanisms of ischemia/reperfusion tissue injury, myocardial stunning, infarction, hibernation and the effects of aging.
- Alterations in regional function and flow and perfusion/contraction relations; postischemic coronary vascular abnormalities; development of collateral circulation in response to myocardial ischemia.
- Myocardial ischemia-induced changes in gene expression including analysis of DNA arrays including myocardial ischemia induced apoptosis.
- Prevention, and treatment of post-ischemic ventricular remodeling and/or inflammation. Prevention and treatment approaches may include pharmacological, gene therapeutic, preconditioning, stem cell and other cellbased approaches.
- Organ preservation during cardiac surgery including transplantation and during cardiac arrest and resuscitation.
- Signal transduction mechanisms of myocardial ischemia/reperfusion injury, preconditioning, and inflammation, including changes in receptor function, kinase activity, and transcription factor activity.
- Pathophysiology and mechanism of myocardial remodeling and/or inflammation in response to ischemia/reperfusion.
- Role of reactive oxygen species, nitric oxide and other reactive nitrogen species, cytokines, chemokines, and white blood cells in myocardial ischemia/reperfusion injury.

- Metabolism and energetics in normal myocardium and in acquired heart disease: carbohydrate and lipid metabolism, glycolysis, oxidative phosphorylation, substrate interaction, regulation of substrate transport and fluxes, mitochondrial function.
- Insulin action and signaling in the myocardium including diabetic cardiomyopathy.
- Regulation of coronary flow in normal and diseased states.

Shared Interests Within the IRG:

There is shared interest in arrhythmias, mediators of inflammation, oxidative stress, nitric oxide biology, signaling, gene regulation, cell-based cardiac repair, and angiogenesis with other study sections in this IRG. Assignment to MIM will be on the basis of a primary focus on myocardial ischemia/reperfusion injury and on the repair of its sequelae. Specific shared interest may occur with applications dealing with:

- <u>Electrical Signaling, Ion Transport and Arrhythmias (ESTA)</u>: Altered electrical behavior in acquired heart disease; e.g. remodeling related to ischemia, may be assigned to ESTA Studies that examine ventricular remodeling following myocardial infarction are appropriately assigned to MIM.
- Cardiac Contractility, Hypertrophy, and Function (CCHF): Systolic and diastolic dysfunction and heart failure, including metabolic adaptations are appropriate for assignment to CCHF. When transplantation is studied only in relation to assessment of myocardial function, applications may be assigned to CCHF. Transplant related organ preservation is appropriately assigned to MIM. Also, when arrhythmias are studied as an etiology of heart failure and myocardial remodeling, including therapeutic effects of pacing on ventricular hemodynamics, the application is appropriately assigned to CCHF. Applications on metabolic studies relating to ischemia-reperfusion and arrhythmias are appropriately assigned to MIM. Studies that examine ventricular remodeling following myocardial infarction are also appropriately assigned to MIM.
- <u>Hypertension and Microcirculation (HM):</u> Applications that examine regional hemodynamics in relation to ischemia are appropriately assigned to HM. In general, studies that focus on coronary circulation would be assigned to MIM.
- Atherosclerosis and Inflammation of the Cardiovascular System (AICS): Transplantation biology including transplant related arrhythmias, graft vasculopathy, atherosclerosis, and transplant immunobiology are appropriately assigned to AICS. Aspects of vascular biology related directly to processes of vascular inflammation; atherogenesis and atherosclerosis regression will also be assigned to AICS. Transplant related organ preservation is more appropriately assigned to MIM. Applications that study inflammation of the myocardium secondary to ischemia and the role of reactive oxygen and nitrogen species, cytokines, and chemokines in myocardial ischemia/reperfusion injury are appropriately assigned to MIM.
- <u>Clinical and Integrative Cardiovascular Sciences (CICS):</u> Applications that examine myocardial ischemia/reperfusion in the context of focused clinical,

population, and integrative studies may be appropriately assigned to CICS. Studies that are appropriately assigned to MIM focus on the mechanism of myocardial injury and/or myocardial preservation.

- Biology of Development and Aging (BDA) IRG: Studies on aging where the primary focus is on regional and global myocardial ischemia/reperfusion could be assigned to MIM. Studies on the cardiovascular system that are testing hypotheses about mechanisms of aging that affect multiple systems or non-cardiovascular tissues could be assigned to the BDA IRG. Studies on cardiovascular function or properties that are part of studies of multiple agerelated changes in physiology or body composition (e.g., fat, cardiovascular and bone) could be assigned to the BDA IRG
- Biobehavioral and Behavioral Processes (BBBP) IRG: Studies emphasizing the effects of acute or chronic psychological stress on cardiovascular endpoints, including ischemia, may be assigned to the BBBP IRG. Research on psychoneuroimmune and psychoneuroendocrine mechanisms in cardiovascular function, exercise as a moderator of the effects of stress on cardiovascular function, and interactions between emotion, personality, psychopathology and cardiovascular function (including reactivity) may be assigned to the BBBP IRG. Applications on the diseases, disorders, or functional consequences of behaviors that contribute to myocardial ischemia could be assigned to MIM.
- Immunology (IMM) IRG: The IMM IRG may be assigned applications where the focus is on the immune system. Studies of inflammation in response to myocardial ischemia/reperfusion could be appropriate for review in MIM.
- Endocrinology, Metabolism, Nutrition and Reproductive Sciences (EMNR) IRG:
 Proposals that focus primarily upon general glucose or lipid metabolism, or the
 effects of obesity, diabetes, or dietary changes on the whole body or multiple
 organ systems may be assigned to the EMNR IRG. Applications dealing primarily
 with the effects of insulin or diabetes on myocardial metabolism or blood flow
 may be assigned to MIM.
- <u>Surgical Sciences</u>, <u>Biomedical Imaging and Bioengineering (SBIB) IRG</u>: Studies
 of myocardial ischemia/reperfusion injury associated with cardiac surgery or
 cardiopulmonary bypass can be appropriately assigned either in the SBIB IRG or
 in MIM, with MIM focused more on cardiovascular evaluation of surgical or
 bypass procedures.
- <u>Neuroscience (MDCN, IFCN, and BDCN) IRGs:</u> Studies of cardiac arrest and resuscitation represent a shared interest. Studies that are appropriately assigned to MIM focus on the mechanism of myocardial injury and/or myocardial preservation whereas, those applications more focused on neurological function would be assigned to one of the neuroscience IRGs.

Hypertension and Microcirculation Study Section (HM) Study Section

The Hypertension and Microcirculation (HM) study section reviews applications involving basic and applied aspects of blood pressure regulation with focus on the physiology of blood pressure regulation and pathogenesis of hypertension as well as blood pressure elevation with aging. It includes studies on cell surface receptors and signaling processes, endogenous vasoactive substances, including the renin-angiotensin system, reactive oxygen species, and their mechanisms of action as related to hypertension, regional hemodynamics, lymphatic circulation, and microcirculation.

Specific areas covered:

- Blood pressure regulation and systemic hypertension. Studies may focus on central or peripheral nervous and endocrine systems, and kidneys and address primary regulators of blood pressure or end organ effects. Mechanisms involving regulation of renal hemodynamic, renal tubular transport, or paracrine, autocrine, or intracrine function, and hormonal/humoral agents produced by the kidney (and other organs) such as renin/angiotensin, dopamine, kallikreins, eicosanoids, nitric oxide and reactive oxygen/nitrogen species when the primary focus is on systemic hypertension.
- Molecular/cellular/biochemical/genetic studies of hypertension. Genetic linkage and association studies or candidate genes analyses in humans and animal models of genetic hypertension. Generation of hypertension models by transgenic/knockout and gene transfer approaches, surgical, drug or hormonal intervention and environmental influences. Methodologies in the measurement and recording of blood pressure.
- Regulation and signaling of adrenergic receptors and G-protein coupled receptors, including activation and regulation of the relevant phospholipases, kinases, phosphatases,cyclases, arrestins and other adaptor and effector proteins as related to hypertension, regional and microcirculation, and lymphatic flow.
- Regional measurements of blood flow including cerebral, splanchnic, skin, skeletal muscle, vasa vasorum, and renal vessels (excluding pulmonary circulation, IRG 19). Microcirculatory functions, including rheology, capillary pressure and fluid exchange and nutrient delivery; arteriole/vein/venule and endothelial cell function.
- Mechanotransduction, contractile and mechanical properties of smooth muscles, vascular permeability, autoregulation, response to metabolism, blood-brain barrier. Modulation of flow by nitric oxide, other vasoactive agents, smooth muscles, ion channels, and gap junctions, and modification of flow by gene transfer. Structural adaptation and remodeling of the vascular system in response to hypertension, e.g., increased peripheral resistance and microvascular rarefaction.
- Lymphatics include functional biology, mechanisms of fluid exchange, propulsion
 of lymph and lymphatic tone, pathophysiological processes contributing to
 primary and secondary lymphedema, and treatment of lymphedema.

Shared Interest within the IRG:

There is a shared interest in neural regulation of blood pressure, reactive oxygen/nitrogen species, receptors, cell biology, and signaling with other study sections in this IRG. Assignment to HM will be appropriate when the primary focus is on the mechanism, diagnosis or treatment of hypertension. Specific shared interest may occur with applications dealing with:

- Vascular Cell and Molecular Biology (VCMB): VCMB focuses on studies of the microcirculation at the cell and molecular levels. Applications addressing integrated and regional microvasculature function are more appropriately assigned to HM.
- Myocardial Ischemia and Metabolism (MIM): Studies that focus on coronary circulation will be assigned to MIM. In most cases, regional blood flow, microcirculation, lymphatic flow and function will be assigned to HM.
- <u>Clinical and Integrative Cardiovascular Science (CICS)</u>: Patient oriented research on hypertension may be assigned to CICS.

- Molecular Approaches to Cell Function and Interactions (MACFI) IRG: Shared interests involve cellular or molecular examination of hypertension and microcirculation. When the focus is a general cellular or molecular understanding, assignment could be to the MACFI IRG. When the focus is an understanding of the biology and physiology of the cardiovascular system, assignment could be to HM
- Genes, Genomes & Genetics (GGG) IRG: Shared interests involve genetic analysis of hypertension and microcirculation. Studies of the genetic analyses of mechanisms of blood pressure regulation and hypertension could be assigned to HM. Studies of quantitative genetics, genetic epidemiology and genetic analysis of complex traits, and genetically engineered animals with an emphasis on genetics rather than mechanisms of blood pressure regulation and hypertension may be assigned to the GGG IRG.
- Health of the Population (HOP) IRG: Applications in which the primary outcomes are population studies related to demographics or epidemiology may generally be assigned to the HOP IRG. Applications on the diseases, disorders, or functional consequences of behaviors could be assigned to HM.
- Risk, Prevention, and Health Behavior (RPHB) IRG: Behavior modification directed toward the prevention and treatment of cardiovascular diseases, including psychological aspects, could be assigned to the RPHB IRG. Applications on the diseases, disorders, or functional consequences of behaviors could be assigned to HM.

- <u>Biobehavioral and Behavioral Processes (BBBP) IRG:</u> Studies emphasizing the effects of acute or chronic psychological stress on cardiovascular endpoints, including blood pressure, may be assigned to the BBBP IRG. Research on psychoneuroimmune and psychoneuroendocrine mechanisms in cardiovascular function, exercise as a moderator of the effects of stress on cardiovascular function, and interactions between emotion, personality, psychopathology and cardiovascular function (including reactivity) may be assigned to the BBBP IRG. Applications on the diseases, disorders, or functional consequences of behaviors that lead to hypertension could be assigned to HM.
- Endocrinology, Metabolism, Nutrition and Reproductive Sciences (EMNR) IRG:
 In general, applications studying hormonal regulatory mechanisms where the
 primary focus is on systemic or regional circulation, or hypertension, including
 preclampsia, could be assigned to HM. Basic or clinical studies that focus
 primarily on the role of hormones may be assigned to the EMNR IRG.
 Applications that directly relate to maternal and fetal cardiovascular physiology
 and disease could also be assigned to the EMNR IRG.
- Respiratory Sciences (RES) IRG: In general applications on regional blood flow could be assigned to HM. Pulmonary blood flow studies would in general be assigned to the RES IRG.
- Renal and Urological Sciences (RUS) IRG: Assignment of applications as they relate to hypertension, including the role of renal hemodynamics, tubular function, and renal humoral/hormonal agents, may be made to either the HM or the RUS IRG based on the central focus of the study. However, clinical studies of hypertension would be assigned to the CVS IRG. Renal hemodynamics, tubular function, and renal humoral/hormonal agents as they affect other aspects of renal function may be assigned to the RUS IRG. Hypertension associated with renal insufficiency or end-stage renal disease would also be assigned to the RUS IRG.
- Brain Disorders and Clinical Neuroscience (BDCN) IRG: Studies dealing with cerebral circulation and hemodynamics may be assigned to HM. Studies that focus on cerebral blood flow and metabolism in the context of neuroimaging for analysis of brain and spinal cord disease or injury, or the functional consequences of ischemia, hypoxia, stroke, or hypoxia on brain or spinal cord function, could be assigned to the BDCN IRG.

Atherosclerosis and Inflammation of the Cardiovascular System (AICS) Study Section

The Atherosclerosis and Inflammation of the Cardiovascular System (AICS) study section reviews applications involving both basic and applied science related to aspects of inflammation of the vascular system with a focus on atherosclerosis, diabetes, transplantation, aging, autoimmunity and infection. This study section will review applications on the pathobiology of the blood vessels leading to atherogenesis, its reversal and prevention. A major contributor to atherogenesis is hyperlipidemia, involving lipids, lipoproteins and their oxidation derivatives. Atherosclerosis is a chronic

inflammatory disease. Thus studies involving inflammatory mediators, cytokines, chemokines, cell signaling, cell migration, and reactive oxygen and nitrogen species and their impact on the cardiovascular system are appropriate. Major risk factors such as diabetes will be emphasized at two levels, the generation of hyperlipidemia and the responses of the vessel wall.

Specific Area Covered By AICS:

- Signaling in the vascular wall; immune mechanisms in vascular inflammation; cytokines, chemokines, cell signaling, reactive oxygen and nitrogen species influencing the vessel wall; macrophages and T cell activation in the cardiovascular system; transplantation immunology related to cardiovascular disease.
- Reactive oxygen and nitrogen species of LDL and in vascular injury including nitric oxide to form peroxynitrite.
- Hepatic lipoprotein metabolism; structure and function of apolipoproteins, lipid metabolizing enzymes and receptors; gene expression and regulation.
- Reverse lipid transport; apoproteins E and A-I; HDL; cell surface molecules in lipid efflux; ABC transporters.
- Lipoprotein interaction with vascular cells; LDL modification and oxidation; LDL interaction with monocyte-macrophage forming foam cells; LDL interaction with matrix components; vascular cell surface receptors for lipoproteins.
- Genetics of lipoprotein metabolism; genetics of responsiveness of cells and enzymes involved in atherogenesis.
- Therapeutic strategies for hyperlipidemia, inflammation and cholesterol disposal; gene therapy; hormone replacement therapy.
- Animal models of atherosclerosis, diabetes, vasculitis, infection or lipid metabolic disorders (inherited or acquired).
- Stem cells; origin of cells of atherosclerotic plaque and cardiovascular inflammatory foci
- Regression of atherosclerosis; plaque stabilization; metalloproteinases; cell and matrix remodeling.
- Lipid mediators in vascular wall inflammation; arachidonic acid metabolites.
- Pro- and anti-inflammatory mechanisms in vessel wall; nuclear hormone receptors; Peroxisome Proliferator Activated Receptor (PPAR) and Liver X Receptor (LXR); sterol and fatty acid ligands.
- Insulin and diabetes effects on lipoprotein metabolism in the liver; lipid and lipoprotein metabolism influencing hepatic insulin action.
- Insulin action and signaling in the vessel wall; insulin resistance.
- Infective agents in promoting vessel wall inflammation.
- Viral or autoimmune myocarditis, Chagas disease, rheumatic heart disease, and other infections of the cardiovascular system, with the exception of transplantassociated infections.

Shared Interests Within the IRG:

There is shared interest in the pathobiology of atherosclerosis with other sections in this IRG. Assignment to AICS will be on the basis of a primary focus on atherosclerosis as an inflammatory process and on diabetes. Specific shared interest may occur with applications dealing with:

- <u>Cardiac Contractility</u>, <u>Hypertrophy</u>, <u>and Function (CCHF)</u>: When transplantation is studied only in relation to assessment of myocardial function, applications may be assigned to CCHF. Applications that study inflammation of the myocardium secondary to ischemia and the role of reactive oxygen and nitrogen species, cytokines, and chemokines in myocardial ischemia/reperfusion injury are appropriately assigned to AICS.
- <u>Vascular Cell and Molecular Biology (VCMB):</u> When the emphasis is on the biology of the endothelium or vascular smooth muscle cell, then VCMB is appropriate. Studies of atherogenesis or vasculitis are more appropriately assigned to AICS. Vascular remodeling related to the refashioning of the atherosclerotic plaque will be assigned to AICS.
- Myocardial Ischemia and Metabolism (MIM): Transplant related organ preservation is appropriately assigned to MIM. Applications that study inflammation of the myocardium secondary to ischemia and the role of reactive oxygen and nitrogen species, cytokines, and chemokines in myocardial ischemia/reperfusion injury are also appropriately assigned to MIM. Transplantation biology including transplant related arrhythmias, graft vasculopathy, atherosclerosis, and transplant immunobiology are more appropriately assigned to AICS. Aspects of vascular biology related directly to processes of vascular inflammation, atherogenesis and atherosclerosis regression will also be assigned to AICS.
- Hypertension and Microcirculation (HM): Although a well recognized risk factor for atherosclerosis, applications that focus on hypertension may be more appropriately assigned to HM.
- Clinical and Integrative Cardiovascular Sciences (CICS): Patient-oriented research applications that focus on genetics and mechanisms involved in the modification of risk factors (such as lipid dysfunction) may be more appropriately assigned to CICS.

- Genes, Genomes & Genetics (GGG) IRG: Studies of the genetic analyses of mechanisms of lipoprotein metabolism or atherogenesis could be assigned to AICS. Studies of quantitative genetics, genetic epidemiology and genetic analysis of complex traits, and genetically engineered animals with an emphasis on genetics rather than mechanisms of lipoprotein metabolism or atherogenesis may be assigned to the GGG IRG.
- Biology of Development and Aging (BDA) IRG: Studies on aging where the
 primary focus is on atherosclerosis and inflammation of the cardiovascular
 system could be assigned to AICS. Studies on the cardiovascular system that
 are testing hypotheses about mechanisms of aging that affect multiple systems
 or non-cardiovascular tissues could be assigned to the BDA IRG. Studies on
 cardiovascular function or properties that are part of studies of multiple age-

related changes in physiology or body composition (e.g., fat, cardiovascular and bone) could be assigned to the BDA IRG

- Health of the Population (HOP) IRG: Applications in which the primary outcomes are population studies related to demographics or epidemiology may generally be assigned to the HOP IRG. Applications on the diseases, disorders, or functional consequences of behaviors could be assigned to AICS.
- Risk, Prevention, and Health Behavior (RPHB) IRG: Behavior modification directed toward the prevention and treatment of cardiovascular diseases, including psychological aspects, could be assigned to the RPHB IRG. Applications on the diseases, disorders, or functional consequences of behaviors could be assigned to AICS.
- Immunology (IMM) IRG: The IMM IRG may be assigned applications concerning the etiology and pathogenesis of organ-specific and systemic autoimmune diseases or transplantation, particularly when the focus is on the immune system. Studies of the immunology of cardiac transplantation or bypass surgery and inflammation of the cardiovascular system as related to atherosclerosis, diabetes, autoimmune myocarditis and other immune-related cardiovascular inflammations could be assigned to AICS when the focus is on the function of the cardiovascular system. AICS is complementary to the IMM IRG with respect to those applications requiring expertise in pathogenic effector mechanisms and specific factors or structures relevant to target organ damage and repair. Similarly, the IMM IRG is complementary to AICS with respect to those applications requiring expertise in immunopathogenic mechanisms. Areas of unavoidable shared interest such as the immunology of cardiac transplantation would be resolved according to the central focus of the application.
- Infectious Diseases and Microbiology (IDM) IRG: Studies of infectious diseases directly related to cardiovascular system injury, inflammation and function may be assigned to AICS. Studies that focus on the pathogen rather than their effect on the cardiovascular system may be assigned to the IDM IRG.
- Endocrinology, Metabolism, Nutrition and Reproductive Sciences (EMNR) IRG:
 Proposals that focus primarily upon lipid metabolism, or the effects of obesity,
 diabetes, or dietary changes on the whole body or multiple organ systems may
 be assigned to the EMNR IRG. Applications dealing primarily with the role of
 lipids in the inflammation of the vascular system, particularly atherosclerosis,
 could be assigned to AICS.

Digestive Sciences (DIG) IRG: Applications on the biochemistry of elevated plasma lipids and lipoproteins in the intestine and liver may be assigned to AICS when the focus is on atherosclerosis and inflammation in the cardiovascular system. Applications dealing with cholesterol and lipid metabolism as it relates to bile salt metabolism and excretion, and the role of cytokines and nitric oxide in the pathogenesis of liver diseases could be assigned to the DIG IRG.

Clinical and Integrative Cardiovascular Sciences (CICS) Study Section

The Clinical and Integrative Cardiovascular Sciences (CICS) study section will consider research applications concerned with basic and clinically oriented research, including multiple organ systems ranging from the cell to whole animal/human research involving cardiovascular regulation. Specific areas of interest in this context include exercise, neural control, patient oriented studies, including surgery and pediatrics, and prevention. Patient oriented research is defined as studies involving investigation of the cardiovascular system of humans, including autonomic physiology and exercise cardiovascular studies. Large clinical trials that focus on outcomes may be assigned to CICS. Applications involving randomized multi-center clinical trials are not appropriate for this study section.

Specific areas covered by CICS:

- Human clinical studies, including pediatric populations, of mechanisms and consequences of disease. Investigations may include coronary physiology and pharmacology, cardiac electrophysiology, regional circulations, hemodynamic studies, cardiac mechanics and cardiovascular genetic studies. Disease states can include cardiac or vascular ischemia, hypertension, diabetes, thyroid disease, atherosclerosis or hypercholesterolemia.
- Clinical, population or integrative, whole animal studies of the responses of the cardiovascular system to trauma or surgery, including arrhythmias associated with cardiac surgery or cardiopulmonary bypass, the use of stents, pacemakers, etc., in cardiovascular injury and repair, and myocardial ischemia/reperfusion injury.
- Environmental stresses. Smoking, altitude, heat, cold, environmental pollution in patients ranging from childhood to adolescence, adult, pregnancy and aging.
- Allopathic and alternative or complementary therapies, excluding large multicenter clinical trials and surveys or studies confined to tissue analysis.
- Exercise. Human and animal models investigating the influence of acute and chronic exercise on cardiac and vascular smooth muscle, neural and humoral systems involved in cardiovascular regulation, vascular endothelial function, specific regional circulations, and gene expression in cardiovascular system may be included. In addition, studies of the adaptive responsiveness of cardiac mechanical, contractile, and metabolic function to acute and chronic exercise in both human and animal models are included.

- Modulation of cardiovascular responses and adaptations by disease and environment. Disorders, such as atherosclerosis, diabetes, ischemia, hypertension, environmental or modifying conditions, and stimuli, such as microgravity, smoking, pollutants, altitude, bed rest, aging, neonatal, maternal and deconditioning, among others, are included.
- Neural control of the cardiovascular system in health and disease. This includes autonomic physiology involving all aspects of reflex arcs (including afferent, central neural integration and efferent/effector organ. Mechanisms of afferent activation of mechano- and chemosensitive sensory endings. Central mechanisms, including anatomy, physiology, pharmacology and receptor mechanisms from the organ to subcellular elements, including gene expression, interactions between brain stem and higher brain areas for long and short loop reflexes, and efferent or autonomic regulation.
- Study of Prevention. This includes modification of cardiovascular risk factors that
 potentially influence cardiovascular function and neural control of cardiovascular
 function. Examples could include alterations of glycemic state, blood pressure or
 lipids or cessation of smoking on cardiovascular function. Pharmacological,
 dietary and lifestyle modifications of these risk factors may be included.
 Conventional, alternative or complementary therapies will be reviewed.

Shared Interests Within the IRG:

There is a shared interest in the study of clinical cardiovascular physiology and pathology with other study sections in this IRG. Clinical trials of small numbers of patients that investigate mechanisms involving particular expertise on other study sections within the IRG may be assigned to these study sections. For example, studies of polygenic cardiovascular diseases may be assigned to CICS, while monogenic studies may be assigned to one of the other cardiovascular sciences study sections.

- <u>Cardiac Contractility, Hypertrophy and Failure (CCHF):</u> Clinical, population, and integrative studies may be more appropriately assigned to CICS.
- <u>Electrical Signaling, Ion Transport and Arrhythmias (AICS)</u>: Applications that deal with the mechanisms of arrhythmogenesis are the purview of ESTA, while CICS may more appropriately be assigned those that are outcome-based.
- <u>Vascular Cell and Molecular Biology (VCMB):</u> VCMB focuses on studies of the microcirculation at the cell and molecular levels. Applications addressing integrated microvasculature function are more appropriately assigned to CICS.
- Myocardial Ischemia and Metabolism (MIM): Studies that are appropriately assigned to MIM focus on the mechanism of myocardial injury and/or myocardial preservation. Applications that examine myocardial ischemia/reperfusion in the context of focused clinical, population, and integrative studies may be more appropriately assigned to CICS.
- Hypertension and Microcirculation (HM): Mechanism based research belongs to HM, whereas patient oriented research on hypertension may be preferentially assigned to CICS.

Atherosclerosis and Inflammation of the Cardiovascular System (AICS): While
applications on the genetics and mechanism of atherosclerosis should be
directed to AICS, patient-oriented research applications that focus on genetics
and mechanisms involved in the modification of risk factors (such as lipid
dysfunction) may be more appropriately assigned to CICS.

- Biology of Development and Aging (BDA) IRG: Studies on aging where the
 primary focus is on clinical studies of the cardiovascular system could be
 assigned to CICS. Studies on the cardiovascular system that are testing
 hypotheses about mechanisms of aging that affect multiple systems or noncardiovascular tissues could be assigned to the BDA IRG. Studies on
 cardiovascular function or properties that are part of studies of multiple agerelated changes in physiology or body composition (e.g., fat, cardiovascular and
 bone) could be assigned to the BDA IRG.
- Health of the Population (HOP) IRG: Applications in which the primary outcomes are population studies related to demographics or epidemiology may generally be assigned to the HOP IRG. Applications on the diseases, disorders, or functional consequences of behaviors could be assigned to CICS.
- Risk, Prevention, and Health Behavior (RPHB) IRG: Behavior modification directed toward the prevention and treatment of cardiovascular diseases, including psychological aspects, could be assigned to the RPHB IRG. Applications on the diseases, disorders, or functional consequences of behaviors could be assigned to CICS.
- <u>Biobehavioral and Behavioral Processes (BBBP) IRG:</u> Studies emphasizing the effects of acute or chronic psychological stress on cardiovascular endpoints, including blood pressure, cardiovascular disease, and ischemia may be assigned to the BBBP IRG. Research on psychoneuroimmune and psychoneuroendocrine mechanisms in cardiovascular function, exercise as a moderator of the effects of stress on cardiovascular function, and interactions between emotion, personality, psychopathology and cardiovascular function (including reactivity) may be assigned to the BBBP IRG. Applications on the diseases, disorders, or functional consequences of behaviors could be assigned to CICS.
- Hematology (HEM), Endocrinology, Metabolism, Nutrition and Reproductive Sciences (EMNR), Respiratory Sciences (RES), Renal and Urological Sciences (RUS), and Integrative, Functional and Cognitive Neurosciences (IFCN) IRGs: When the primary emphasis of clinical studies is on the cardiovascular system, including its response to neural control, applications may be assigned to CICS. When the primary emphasis of a multi-system clinical study is not on the cardiovascular system, the application could be assigned to the relevant organ system IRG.

- Musculoskeletal, Oral and Skin Sciences (MOSS) IRG: The MOSS IRG and CICS have complementary roles and mutual interests. (1) In general, the influence of exercise on the cardiovascular system would be assigned to CICS. Similar studies where the primary focus is on the musculoskeletal system could be assigned to the MOSS IRG. Studies that focus on blood flow in skeletal muscle in response to exercise would be assigned on the basis of the central interests of the application.
- Renal and Urological Sciences (RUS) IRG: In general, clinical protocols dealing
 with hypertension would be assigned to CICS. Clinical protocols dealing with
 other renal or urological disorders would be assigned to the RUS IRG.
- Surgical Sciences, Biomedical Imaging and Bioengineering (SBIB) IRG: (1)
 Organ preservation and graft rejection-related arrhythmias, and surgical
 interventions to treat valve dysfunction, may be assigned to the SBIB IRG.
 Patient oriented or whole animal research on the responses of the cardiovascular
 system to trauma, surgery, or other physiologic stress may be assigned to CICS.
 (2) Studies of arrhythmias associated with cardiac surgery or cardiopulmonary
 bypass can be appropriately assigned either in the SBIB IRG or CICS, with CICS
 focused more on cardiovascular evaluation. (3) Patient-oriented or whole
 animal research on the use of stents, pacemakers, etc., in cardiovascular injury
 and repair are appropriate for CICS. Those involving more general aspects of
 bioengineering could be assigned to SBIB IRG. (4) Patient-oriented or whole
 animal studies of myocardial ischemia/reperfusion injury associated with cardiac
 surgery or cardiopulmonary bypass can be appropriately assigned either in the
 SBIB IRG or to CICS, with CICS focused more on cardiovascular evaluation of
 surgical or bypass procedures.